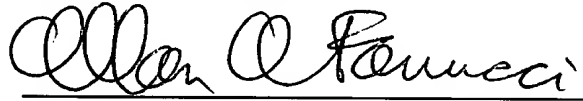


No fee is believed to be due for entry of this Preliminary Amendment.
However, if any fee should be required, please charge such fee to Pennie & Edmonds LLP
Deposit Account No. 16-1150.

Date

7/28/99

Respectfully submitted,



Allan A. Fanucci

(Reg. No. 30,156)

PENNIE & EDMONDS LLP

1667 K Street, N.W.

Washington, DC 20006

(202) 496-4400

09355363 "072899

A

Cancel
by A
#4/
Sub
Spec.

MODIFYING AND SUPPLYING LIQUID NUTRITIONAL FEEDING

TECHNICAL FIELD

The present invention relates to an apparatus and method for modifying and feeding a liquid nutritional feeding composition, in particular to its modification by adding a beneficial agent to the liquid feeding composition, before feeding said liquid feeding composition.

BACKGROUND

It is known to enterally or intravenously feed liquid nutrition to patients who are not able to eat by themselves. Such liquid meals are normally provided in hangable containers such as bottles or plastic bags and are fed from the containers through a tube to the patient. A number of different liquid nutritional feeds are available for the ^{varying} ~~variation~~ of the nutritional intake of the patient. Nevertheless, there is a need ^{to} for ~~a~~ ^{tailor} ~~tailoring~~ of the liquid meals to the patient's individual needs. This is known to be done by adding beneficial agents such as for example nutrients, probiotics and medicaments to the liquid nutritional feed. The adding of such beneficial agents should, for some applications, preferably take place just before the feeding starts as a premature mixing of the liquid nutritional feed and the beneficial agent may ^{decrease} ~~increase~~ considerably the quality and shelf-life of the liquid nutritional feed.

The liquid meals provided in hangable containers such as bottles or plastic bags are generally aseptically processed or terminally retorted before use. This

increases the shelf life of the liquid meal. For providing an aseptic feed to the patient, the container is connected directly via a feeding tube or line to the patient. Any opening of the system for adding a
5 beneficial agent increases the risk for bacterial growth or contamination. A closed-line system for the modifying and feeding of patients is therefore desirable.

The prior art discloses closed-line systems wherein a
10 liquid nutritional feeding composition is ^{passed} ~~passing~~ through a chamber comprising a beneficial agent ^{before entering} ~~to~~ the patient feeding line. The beneficial agent is mixed or dissolved in the liquid nutritional feeding composition when it is ^{passes} ~~is passing~~ through the chamber.

15

In order to homogenise the feed to the patient in this type of feeding system and thus prevent an over concentration of the beneficial agent, it is necessary to control the release of the beneficial agent.
20 Consequently, a beneficial agent in controlled release form is used, i.e. an agent the solubility of which is delayed or retarded. For example, ~~the~~ supplying of the liquid nutritional feed releases the beneficial agent over a period of 2 to 24 hours. Furthermore, although
25 the controlled release form allows the beneficial agent to be released over a period, in-homogeneity may be experienced in the start-up phase due to the protective coating on the beneficial agents.

09355363 "072899

SUMMARY OF THE INVENTION

It is an object of the invention to provide an improved system for modifying and feeding a homogeneous mixture of a liquid nutritional feed and a beneficial agent. In particular to provide a delivery ^{apparatus} useable ^{with a} ~~for the~~ beneficial agent in a non-controlled release form.

It is a further object of the invention to provide a closed-line system for modifying and feeding a mixture of a liquid nutritional feed composition and a beneficial agent ^{by} allowing the operations to take place without opening the system to bacteria or contamination.

Accordingly, in a first aspect, the invention concerns an apparatus for modifying and feeding a liquid nutritional feeding composition comprising,

a chamber for receiving a beneficial agent for modifying a liquid nutritional feeding composition, the chamber having an inlet connectable to a container containing the nutritional feeding composition and an outlet connectable to a feeding means, and

a pumping means associated with the chamber for pumping the nutritional feeding composition from the container into the chamber and back to the container for mixing the beneficial agent into the nutritional feeding composition.

Thus, the present invention provides an apparatus for modifying and feeding a liquid nutritional feeding composition which allows the addition of a beneficial agent to the liquid feed immediately before the feeding

093536-072399

commences, which addition of the beneficial agent is done without an opening and reclosing of the system. The mixing of the beneficial agent ^{and} ~~to~~ the liquid feeding is conducted by pumping means arranged to pump liquid feed
5 from the container into the chamber and liquid and beneficial agent back into the container. After end mixing, the chamber is connected to feeding means for feeding of the mixture to the patient.

10 It has been found that a homogeneous modification and feeding can be obtained with the feeding system according to the invention. Furthermore, it has been found that the mixture of liquid feed and the beneficial agent is stable during 48 hours' feeding.

15 In a particularly advantageous embodiment of the invention the pumping means is adapted to vary the volume of the chamber being used for pumping of the nutritional feeding composition. Especially preferred is
20 an embodiment of the invention wherein the chamber comprises at least one flexible wall capable of being squeezed and released for pumping of the nutritional feeding composition. For example, ^a ~~the~~ wall of plastic material ^{has} ~~the~~ flexibility ~~of~~ which allows a deformation
25 of the wall.

For the embodiment of the above-mentioned flexible wall type, in order to obtain an appropriate pumping effect and thus limit the number of pumping cycles necessary
30 for the mixing of the beneficial agent with the liquid,

09355363.072899

the chamber should not be too full of the beneficial agent. Conveniently, at least 30% of the volume of the chamber is empty in the un-squeezed state. Preferably, the volume of beneficial agent constitutes from 5% to 5 70%, preferably from 30% to 50% of the volume of the chamber. The limits of the ratio filled and un-filled volume will depend on the solubility of the product.

The liquid nutritional feeding composition is of a 10 conventional type. The liquid nutritional feeding composition may comprise from 0 to 25% protein, from 0 to 50% lipids, and from 0 to 60% carbohydrates. For example, it ^{may} comprises about 15% protein, about 35% lipids, and about 50% carbohydrates. The water content 15 is preferably from 70 to 95% by weight.

The chamber may be delivered as a sealed unit comprising the beneficial agent. Alternatively, the chamber may be filled with the beneficial agent at the location where 20 the treatment is to take place.

The connections between the container, the chamber, and the feeding means are preferably as follows: ^{an} the inlet is provided with a hollow spike for piercing of a port 25 of the container and creating a fluid path for the nutritional feeding composition. The feeding means comprises a hollow spike for piercing the outlet of the chamber and creating a fluid path for the nutritional feeding composition with the beneficial agent. The 30 piercing of the outlet of the chamber is done after end

mixing. The present system of connection allows for ~~an~~ on-line feeding of an aseptic liquid nutritional feeding composition with a beneficial agent.

- 5 The flow ^{from} ~~of~~ the container to and through the feeding tube means may be due to gravity alone, but preferably the flow from the container to and through the feeding tube means is assisted by a pump.
- 10 The beneficial agent is dispersible in the nutritional liquid feed. By dispersible is understood, soluble as well as agents that are suspendable so as to be mixed with the liquid feed and forwarded herewith.
- 15 The beneficial agent or agents is/are ^{for} ~~an~~ e.g., selected from the group consisting of nutrients, probiotics, medicaments and diagnostic tracer or a physiological combination thereof.
- 20 It is preferred that the ~~or each~~ beneficial agent(s) is/are dispersible in the nutritional feeding composition in less than 1 min, more preferably in less than 30 sec.

For beneficial agents that are stable in liquid
 25 conditions, the agents may be provided in liquid form. Even if the beneficial agent is stable in a certain liquid formulation, a mixture of the liquid nutritional feeding composition and the liquid beneficial agent may not be stable for a longer period, thus the apparatus
 30 according to the invention may advantageously be used.

09355363 "072899

For enteral feeding the beneficial agents are cleaned but there is no need for a sterile product. However, for intravenously fed liquid, the beneficial agent must be
5 sterilised.

The beneficial agent preferably comprises nutrients selected from the group consisting of glutamine, vitamins, arginine, fermentable and non-fermentable
10 dietary fibres, enzymes, oligo elements, combinations of amino acids, oligosaccharides, short chain fatty acids, salts, structured lipids, d-cytrinositol, lactoferrin, marine oils, ~~and~~ acidulents, antioxidants, or a combination thereof.

15 The apparatus according to the invention may advantageously be used for enteral or intravenous feeding. For intravenous feeding the beneficial agent is sterilised.

20 In a second aspect, the invention relates to a method for modifying and feeding a liquid nutritional feeding composition comprising,

connecting a chamber, of the kind described above,
25 to a container comprising a liquid nutritional feeding composition,

pumping liquid feeding composition into the chamber, and liquid nutritional feeding composition and the beneficial agent back to the container to mix with
30 the nutritional feeding composition,

09355363 "072899

connecting the feeding means, and
 allowing the modified nutritional feeding
 composition to flow through the chamber into the feeding
 means.

5 BRIEF DESCRIPTION OF THE DRAWINGS

The present invention will now be described in further
 detail by way of examples only with reference to the
 accompanying drawings and examples, in which

Fig. 1 is a principle drawing illustrating enteral
 10 feeding of a patient with an apparatus according to the
 invention,

Fig. 2 is a cross-sectional principle drawing of the
 chamber for receiving a beneficial agent, and

Fig. 3 shows a measure of levels of beneficial agent in
 15 a feed.

DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENTS

Fig. 1 shows an apparatus 1 according to the invention
 arranged for modifying and feeding a liquid nutritional
 feed 6 to a patient, not shown in the drawings. The
 20 apparatus 1 comprises a chamber 3 containing a
 beneficial agent. The chamber 3 is connected to a
 container 5 containing the nutritional feeding
 composition 6 via an inlet 7. An outlet 13 in the
 chamber 3 is connected to feeding tubes 8 and 9 which
 25 serve to lead the modified feeding composition to the
 patient. The feeding tube 9 extends through the nasal
 path and to the stomach of the patient. Pumping means is
 provided in the form of the chamber 3 which has a
 flexible wall structure 12 for pumping the liquid
 30 feeding composition 6 into the chamber 3 and back to the

09455363 "072899

container 5 so as to modify the liquid feeding composition 6. In order to assure attachment between the parts 5, 7, 8, 9 and 13, conventional fastening means 17 and 18 are provided. Furthermore, a pump 10 to assist the flow from the outlet 13 and flow regulation means 11 are provided.

Fig. 2 illustrates a chamber 3 according to the invention. The chamber 3 comprises an inlet 7 and an outlet 13. A chamber wall 12 is provided in a flexible plastic, ^{for} e.g., soft ^{Polyvinyl} Polycy~~nyl~~ Chloride and a rigid lid 14 is made from a harder plastic, ^{for} e.g., hard ^{Polyvinyl} Polycy~~nyl~~ Chloride. In the present embodiment the inlet 7 is defined in the lid 14. The lid 14 may, ^{for} e.g., be sealed onto the wall 12 by ultrasonic welding or provided with threads ⁺ and screwed ⁺ onto the wall 12.

Before use, the chamber 3 the inlet 7 and the outlet 13 are closed by thin membranes 15 and 16. For the initial mixing of a beneficial agent with a liquid feeding composition, the inlet's membrane 15 is first pierced when being connected to the container 5 shown in Fig. 1. Upon end pumping and mixing, the tube feeding 8 of Fig. 1 is to be connected to the chamber 3 which results in a piercing of the outlet's membrane 16.

EXAMPLE 1

Several liquid nutritional feeding compositions are modified and fed by

09355363 072899

1) connecting containers of liquid, feeding to a flexible chamber according to the invention, by piercing the port in the container with the spike of the container,

2) pumping liquid from the container to the chamber and back again by squeezing and releasing the chamber 3 to 5 times, and

3) connecting the feeding means by piercing the outlet of the chamber, thus feeding the modified liquid feed composition to the feeding means. The flow is by gravity or assisted by a pump.

Tests are, for example, carried out ^{by} feeding.

15

1) 12 g glutamine as beneficial agent constituting about 60% of the volume of the chamber with 500 ml or 1 L liquid feed.

2) 1 g pro-biotic as beneficial agent constituting about 5% of the volume of the chamber with 500 ml or 1 L liquid feed.

3) 12 g glutamine mixed with 1 g pro-biotic as beneficial agent constituting in total about 65% of the volume of the chamber with 500 ml or 1 L liquid feed.

The liquid feeds are commercially available products such as Réabilan HN, Réabilan, Sondalis ISO, and Sondalis HP supplied by Nestlé S.A. Switzerland.

09355363 "072899

The modified feed is inspected and characterised as homogeneous.

5 EXAMPLE 2 - Stability

The stability of the mixture of the liquid nutritional feeding composition and the beneficial agent are controlled by the level of beneficial agent ^{as} ~~is~~ measured
10 by means of a calorimetric method (Kit Boehringer).

Mixtures of liquid nutritional feeding composition and beneficial agent are fed and samples are stored ^{for} ~~e.g.~~ 24 hours and 48 hours and the level of beneficial agent is
15 measured.

For example, the stability of Sondalis ISO and Réabilan HN comprising Glutamine are measured over ^{this} ~~a~~ period:

	Sondalis ISO	Réabilan HN
20 T= 0h	12,9 g/l	14,6 g/l
T= 24h	12.6 g/l	13,5 g/l
T= 48h	12.5 g/l	12,9 g/l

The measurements show that the Glutamine is stable above
25 a level of 12 g/l after 48 hours.

EXAMPLE 3 - Homogenisation

^{The} ~~A~~ homogeneity of the modified liquid nutritional feeding
30 composition is controlled by mixing the beneficial agent

09355363 072859

or agents with the liquid nutritional feeding composition by pumping 5 times the liquid into and out of the chamber.

- 5 The feeding tube or line is connected to the chamber and an enteral pump running at 100 ml/h, corresponding to a continuous nutrition (24h/42h).

During the feeding, after each 50 ml fed, the level of
10 beneficial agent is measured by means of a calorimetric method (Kit Boehringer).

Fig. 3 shows the amount of beneficial agent in a feed, in the example in question the beneficial agent is
15 Glutamine in ~~a~~ 500 ml ^{of} in 4 different liquid feeding compositions. It is apparent from the figure that the Glutamine level is ^{homogeneous at} ~~homogeneously~~ about 12-14 g/l during the feeding period.

20 EXAMPLE 4

In order to verify that the geometry of the liquid containing container did not influence the
homogenisation of the modified feed, trials ^{were} ~~are~~
25 conducted with drip-pack, plastic pouches, and glass bottles. No difference in the homogeneity was detected from the various containers.

09355363.072899

CLAIMS

What is claimed is:

1. An apparatus for modifying and feeding a liquid nutritional feeding composition comprising,
 - 5 a chamber for receiving a beneficial agent for modifying a liquid nutritional feeding composition, the chamber having an inlet connectable to a container containing the nutritional feeding composition and an outlet connectable to a feeding means, and
 - 10 a pumping means associated with the chamber for pumping said nutritional feeding composition from the container into the chamber and back to the container for mixing the beneficial agent into the nutritional feeding composition.
- 15 2. An apparatus according to claim 1, wherein the volume of the chamber being alterable for pumping of the nutritional feeding composition.
- 20 3. An apparatus according to either claim 1 or 2, wherein the chamber comprises at least one flexible wall capable of being squeezed and released for pumping of the nutritional feeding composition.
- 25 4. An apparatus according to any of claims 1 to 3, wherein the chamber comprises at least one beneficial agent selected from the group consisting of nutrients, probiotics, medicaments (and diagnostic agents) or a (physiological) combination thereof.

5 6. An apparatus according to any of claims 1 to 4,
wherein the or each beneficial agent is dispersible in
the nutritional feeding composition in less than 30 sec.

8. An apparatus according to any of claims 1 to 7,
wherein the inlet is provided with a hollow spike for
15 piercing of a port of the container and creating a fluid
path for the nutritional feeding composition.

10. Use of an apparatus according to any of claims 1 to
25 9 for modifying and enterally supplying of liquid
nutritional feeding composition.

11. Use of an apparatus according to any of claims 1 to
9 for modifying and intravenous supplying of liquid
30 nutritional feeding composition.

12. A method for modifying and feeding a liquid nutritional feeding composition comprising,

connecting a chamber according to any of claims 1
5 to 2 to a container comprising a liquid nutritional feeding composition,

pumping liquid feeding composition into the chamber and liquid nutritional feeding composition and beneficial agent back to the container to mix the
10 nutritional feeding composition,

connecting the feeding means according to either claims 1 or 9, and

allowing the modified nutritional feeding composition to flow through the chamber into the feeding
15 means.

13. A method according to claim 12, wherein the flow from the container to and through the feeding tube means, is due to gravity.

20

14. A method according to claim 12, wherein the flow from the container to and through the feeding tube means, is assisted by a pump.

658240 07239

ABSTRACT

The present invention relates to an apparatus for modifying and feeding a liquid nutritional feeding composition. Said apparatus comprises 1) chamber (5) for receiving a beneficial agent for modifying a liquid nutritional feeding composition, the chamber having an inlet (7) connectable to a container (5) containing the nutritional feeding composition and an outlet (13) connectable to a feeding means (8,9) and a pumping means associated (3) with the chamber for pumping said nutritional feeding composition from the container into the chamber and back to the container for mixing the beneficial agent into the nutritional feeding composition before connecting the outlet (13) of said chamber to the feeding means (8,9). It is preferred that the chamber (3) comprises at least one flexible wall capable of being squeezed and released for pumping of the nutritional feeding composition. The invention also relates to a method for modifying and feeding a liquid nutritional feeding composition.